Well-Designed Supramolecular Clusters Comprising Triphenylmethylamine and Various Sulfonic Acids

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Organic nanoparticles have attracted considerable research interest in molecular biology and life sciences as well as nanotechnology and materials science because of their unique properties. However, the preparation of nanoparticles with a uniform size has remained an important area of study. Organic synthesis is a reliable method for preparing monodisperse particles. Furthermore, we can prepare homogeneously sized particles more efficiently and in greater amounts by borrowing techniques from supramolecular chemistry. In this paper, we describe that [4+4] ion-pair clusters as an organic nanoparticle composed of triphenylmethylammonium (TPMA) and sulfonate ions can be obtained easily and efficiently in the solid state and in solution with many different sulfonic acid derivatives.

A crystallographic study revealed that four sterically hindered TPMA and four monosulfonic acid assemble into a [4+4] ion-pair cluster, through a cubic hydrogen-bonded network, and that the binary components are located alternately at the apex of the cube (Fig.1).

A total of twelve phenyl groups, present in the four triphenylmethyl groups, cover the hydrophilic core and form a barrier. Within the core, eight central atoms, four nitrogen and four sulfur atoms, form a cube. This characteristic structure, similar to a reverse micelle, contributes to the high solubility of the ammonium–sulfonate salt in nonpolar solvents. Surprisingly, a wide range of sulfonic acids yielded clusters. Their preparation is based on the specificity of the combination of the ammonium and sulfonate ions; this system is potentially useful for synthesizing organic nanoparticles. The efficiency of formation and the robustness of the clusters are due to three factors: the topology of the hydrogen-bonded network; the steric effect of the substituents; the acidity of the sulfonic acids. These novel clusters have inherent shapes and sizes that are controlled by the substituent on the sulfonic acid (Fig.2). Because of their nanoscale sizes, these clusters may also have potential as a novel organic material.

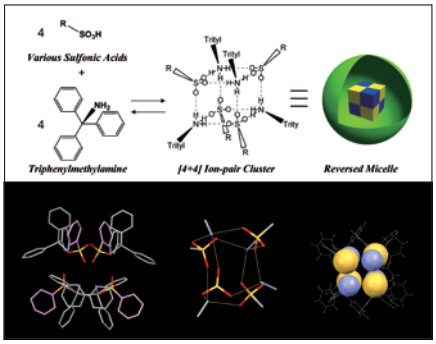

Fig. 1 Fabrication of the [4+4] ion-pair clusters from TPMA and the sulfonic acids.X-ray crystal structure of the supramolecular cluster. Network of hydrogen bonds (yellow dashed lines) and the central elements within the cluster.

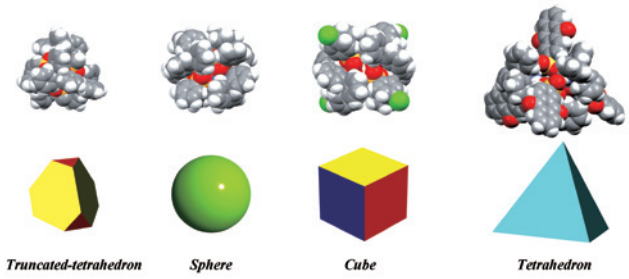

Fig. 2 Space-filling representations and schematic representations of the characteristic shapes of the supramolecular clusters

Intra- and Inter-cellular Signaling Pathways Critical for DNA Vaccine Immunogenicity

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Successful vaccines contain not only protective antigen(s) but also an adjuvant component that triggers innate immune activation and is necessary for their optimal immunogenicity. In the case of DNA vaccines, this consists of plasmid DNA; however, the adjuvant element(s) as well as its intra- and inter-cellular innate immune signalling pathway(s) leading to the encoded antigen-specific T- and B-cell responses remain unclear. Toll-like receptor 9, the only known DNA sensor in immunity essential for immunostimulatory single stranded DNA containing CpG motifs, had been considered to be a critical innate immune receptor for plasmid DNA and to mediate its adjuvant effect on antigen-specific (adaptive) immune responses. On the other hand, this central dogma of DNA vaccine immunogenicity through TLR9 has recently been questioned by the findings that TLR9 KO mice did elicit normal immune responses to DNA vaccines, and that there are TLR9-independent, CpG-DNA-indepenednt innate immune activations.

In this paper, the authors demonstrated *in vivo* that TANK-binding kinase 1 (TBK1), a non-canonical IB kinase, mediates the adjuvant effect of DNA vaccines and is essential for its immunogenicity in mice. Plasmid-DNA-activated, TBK1-dependent signalling and the resultant type-I interferon receptor-mediated signalling was required for induction of antigen-specific B and T cells, which occurred even in the absence of innate immune signalling through a well known CpG DNA sensor—Toll-like receptor 9 (TLR9) or Z-DNA binding protein 1 (ZBP1, also known as DAI, which was recently reported as a potential B-form DNA sensor4). Moreover, bone-marrow-transfer experiments revealed that TBK1-mediated signalling in haematopoietic cells was critical for the induction of antigen-specific B and CD4+ T cells, whereas in non-haematopoietic cells TBK1 was required for CD8+ T-cell induction. These data suggest that TBK1 is a key signalling molecule for DNA-vaccine-induced immunogenicity, by differentially controlling DNA-activated innate immune signalling through haematopoietic and non-haematopoietic cells.

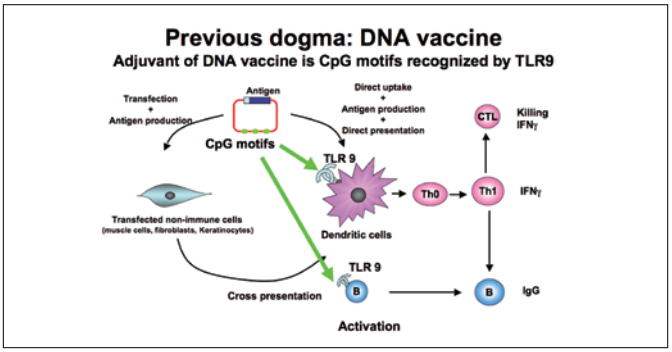

Fig. 1

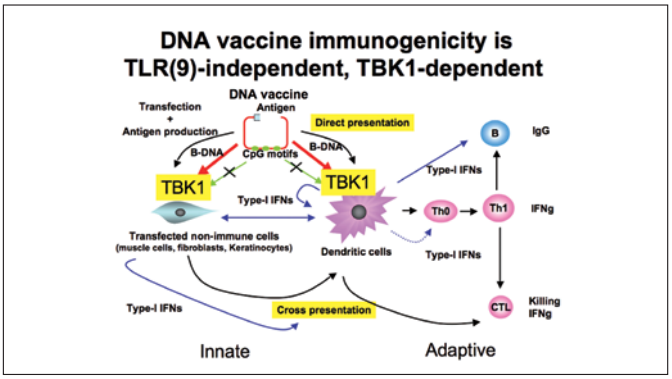

Fig. 2